COMPOSITIONS INCLUDING CD3 ANTIGEN BINDING FRAGMENTS AND USES THEREOF

RELATED APPLICATION

[0001] This application is the U.S. National Stage of PCT/IB2019/055228, filed Jun. 20, 2019, which claims priority under 35 U.S.C. § 119(e) to U.S. Provisional Application 62/687,967 filed Jun. 21, 2018, the entire contents of which are incorporated herein by reference.

SEQUENCE LISTING

[0002] The instant application contains a Sequence Listing which has been submitted electronically in ASCII format and is hereby incorporated by reference in its entirety. Said ASCII copy, created on Dec. 16, 2020, is named 098065-0282 SL.txt and is 129,610 bytes in size.

TECHNICAL FIELD

[0003] The present technology relates generally to the preparation of immunoglobulin-related compositions (e.g., antibodies or antigen binding fragments thereof) that specifically bind CD3 and uses of the same.

BACKGROUND

[0004] The following description of the background of the present technology is provided simply as an aid in understanding the present technology and is not admitted to describe or constitute prior art to the present technology.

[0005] The development of multivalent and multispecific therapeutic proteins with favorable pharmacokinetics and functional activity has been a challenge.

[0006] Bi-specific antibodies capable of targeting and recruiting T cells to tumor cells have been identified and tested for their efficacy in the treatment of cancers. Blinatumomab is an example of a bi-specific anti-CD3-CD19 antibody in a format called BiTE™ (Bi-specific T-cell Engager) that has been identified for the treatment of B-cell diseases such as relapsed B-cell non-Hodgkin lymphoma and chronic lymphocytic leukemia (Baeuerle et al., 12:4941-4944 (2009)). The BiTE™ format is a bi-specific single chain antibody construct that links variable domains derived from two different antibodies. Blinatumomab, however, possesses poor half-life in vivo, and is difficult to manufacture in terms of production and stability.

[0007] Thus, there is an urgent need for improved bi-specific antibodies, capable of targeting T-cells to tumor cells and having improved manufacturability.

SUMMARY OF THE PRESENT TECHNOLOGY

[0008] In one aspect, the present disclosure provides an antibody or antigen binding fragment thereof comprising a heavy chain immunoglobulin variable domain (V_H) and a light chain immunoglobulin variable domain (V_L), wherein (a) the V_H comprises a V_H-CDR1 sequence of GVTFNYYG (SEQ ID NO: 3), a V_H-CDR2 sequence selected from the group consisting of ITRSGGRI (SEQ ID NO: 5) and ITSSGGRI (SEQ ID NO: 14), and a V_H-CDR3 sequence of TLDGRDGWVAY (SEQ ID NO: 4) or TLDGREGWVAY (SEQ ID NO: 156); and/or (b) the V_L comprises a V_L-CDR1 sequence of: TGNIGSNY (SEQ ID NO: 7), a V_L-CDR2 sequence of RND (SEQ ID NO: 9), and a V_L-CDR3 sequence of: QSYSSGFI (SEQ ID NO: 8).

[0009] In one aspect, the present disclosure provides an antibody or antigen binding fragment thereof comprising a heavy chain immunoglobulin variable domain (V_H) and a light chain immunoglobulin variable domain (V_L), wherein (a) the V_H comprises a V_H-CDR1 sequence, a V_H-CDR2 sequence, and a V_H-CDR3 sequence of SEQ ID NO: 155, SEQ ID NO: 157, and SEQ ID NO: 156 respectively, and the V_L comprises a V_L-CDR1 sequence, a V_L-CDR2 sequence, and a V_L-CDR3 sequence of SEQ ID NO: 160, SEQ ID NO: 162, and SEQ ID NO: 161 respectively; (b) the V_H comprises a V_H-CDR1 sequence, a V_H-CDR2 sequence, and a V_H-CDR3 sequence of SEQ ID NO: 115, SEQ ID NO: 117, and SEQ ID NO: 116 respectively, and the V_L comprises a V_L-CDR1 sequence, a V_L-CDR2 sequence, and a V_L-CDR3 sequence of SEQ ID NO: 120, SEQ ID NO: 122, and SEQ ID NO: 121 respectively; (c) the V_H comprises a V_H-CDR1 sequence, a V_H-CDR2 sequence, and a V_H-CDR3 sequence of SEQ ID NO: 185, SEQ ID NO: 187, and SEQ ID NO: 186 respectively, and the V_L comprises a V_L-CDR1 sequence, a V_L-CDR2 sequence, and a V_L-CDR3 sequence of SEQ ID NO: 190, SEQ ID NO: 192, and SEQ ID NO: 191 respectively; (d) the V_H comprises a V_H-CDR1 sequence, a V_H-CDR2 sequence, and a V_H-CDR3 sequence of SEQ ID NO: 135, SEQ ID NO: 137, and SEQ ID NO: 136 respectively, and the V_L comprises a V_L-CDR1 sequence, a V_L-CDR2 sequence, and a V_L-CDR3 sequence of SEQ ID NO: 140, SEQ ID NO: 142, and SEQ ID NO: 141 respectively; (e) the V_H comprises a V_H-CDR1 sequence, a V_H-CDR2 sequence, and a V_H-CDR3 sequence of SEQ ID NO: 175, SEQ ID NO: 177, and SEQ ID NO: 176 respectively, and the V_L comprises a V_L-CDR1 sequence, a V_L-CDR2 sequence, and a V_L-CDR3 sequence of SEQ ID NO: 180, SEQ ID NO: 182, and SEQ ID NO: 181 respectively; (f) the V_H comprises a V_H-CDR1 sequence, a V_H-CDR2 sequence, and a V_H-CDR3 sequence of SEQ ID NO: 145, SEQ ID NO: 147, and SEQ ID NO: 146 respectively, and the V_L comprises a V_L-CDR1 sequence, a V_L-CDR2 sequence, and a V_L-CDR3 sequence of SEQ ID NO: 150, SEQ ID NO: 152, and SEQ ID NO: 151 respectively; (g) the V_H comprises a V_H-CDR1 sequence, a V_H-CDR2 sequence, and a V_H-CDR3 sequence of SEQ ID NO: 125, SEQ ID NO: 127, and SEQ ID NO: 126 respectively, and the V_L comprises a V_L-CDR1 sequence, a V_L-CDR2 sequence, and a V_L-CDR3 sequence of SEQ ID NO: 130, SEQ ID NO: 132, and SEQ ID NO: 131 respectively; (h) the V_H comprises a V_H-CDR1 sequence, a V_H-CDR2 sequence, and a V_H-CDR3 sequence of SEQ ID NO: 65, SEQ ID NO: 67, and SEQ ID NO: 66 respectively, and the V_L comprises a V_L-CDR1 sequence, a V_L-CDR2 sequence, and a V_L-CDR3 sequence of SEQ ID NO: 70, SEQ ID NO: 72, and SEQ ID NO: 71 respectively; or (i) the V_H comprises a V_H-CDR1 sequence, a V_H-CDR2 sequence, and a V_H-CDR3 sequence of SEQ ID NO: 165, SEQ ID NO: 167, and SEQ ID NO: 166 respectively, and the V_L comprises a V_L-CDR1 sequence, a V_L-CDR2 sequence, and a V_L-CDR3 sequence of SEQ ID NO: 170, SEQ ID NO: 172, and SEQ ID NO: 171 respectively.

[0010] In one aspect, the present disclosure provides an antibody or antigen binding fragment thereof comprising a heavy chain immunoglobulin variable domain (V_H) amino acid sequence comprising SEQ ID NO: 1, SEQ ID NO: 10, SEQ ID NO: 20, SEQ ID NO: 30, SEQ ID NO: 53, SEQ ID NO: 63, SEQ ID NO: 73, SEQ ID NO: 83, SEQ ID NO: 93,